

**ABSTRACT**

Provided are methods and compositions useful in detecting protease activity in a sample, as well as methods of identifying agents that modulate protease activity. The methods and compositions provide a modified luciferase polynucleotide sequence and a 5 luciferase polypeptide containing protease recognition sequences, wherein cleavage of the recognition sequence by a protease inhibits luciferase activity. Further provided are methods and compositions for detecting and modulating caspase activity and apoptosis.